MAY - 8 2012

510(k) Summary K102841

Submitted By:	Pantex, Division of Bio-Analysis, Inc. 1701. Berkeley Street Santa Monica, CA 90404 USA (310) 828-7423
Company Contact:	Romulo Garza, Ph.D., President/Senior Scientist
Date Summary Prepared:	4-3-12
Trade Name:	Pantex AM/PM Salivary Cortisol EIA Kit
Common Name:	Enzyme immunoassay, cortisol, salivary
Regulation Number and Panel:	862.1205-Clinical Chemistry
Classification Product Code:	NHG
Classification:	Class II
Substantially Equivalent Device:	K011323 Salimetrics HS Salivary Cortisol EIA Kit Item No. 1-3102 (single) 96 well kit

Device Description:

A. Test principle.
The basis of the Cortisol Enzyme Immunoassay (EIA) is the quantitative relation between ligand concentration and the proportion of Cortisol (analog) enzyme conjugate bound to the antiserum. For example: Cortisol in the calibrators and unknowns compete with Cortisol coupled to peroxidase for antibody binding sites. After incubation, unbound components are washed away. The reaction between Cortisol peroxidase with the substrate (TMB) produces a blue color. The pre-determined time of incubation the reaction is stopped and a yellow color is formed. The optical density (read at 450 nm) is inversely proportional to the cortisol of calibrators, saliva samples and saliva controls.

B. Kit Description.
The kit consists of a 96 well GARGG (Goat Anti-Rabbit Gamma Globulin) coated microplate (12x8 breakable strip wells), seven ready-to-use calibrators (range 0.1-30 ng/ml) of gravimetrically prepared cortisol from a commercial source (Steraloids) and compared and traced to NIST cortisol, low and high controls, anti-Cortisol (rabbit), 10X concentrated Cortisol (analog)-peroxidase, substrate solution, stop reaction solution and 10X concentrated wash solution.

C. Intended Use/Indications for Use:
For the in-vitro diagnostic quantitative determination of free and protein bound salivary cortisol in human saliva as an aid in the assessment of Cushing Syndrome and Addison's Disease. Measurements of cortisol in saliva are used in the diagnosis and treatment of disorders of the adrenal gland.

Predicate Device:
The predicate device for substantial equivalence in this submission is:

Device Name	Salimetrics Salivary Cortisol HS EIA Kit
Company	Salimetrics
510(k) reference	K011323

Technology Comparison:

	Predicate Device: Salimetrics Salivary Cortisol HS EIA Kit (K011323)	New Device: Pantex AM/PM Salivary Cortisol EIA Kit (K102841) pending
Indications for use	For the in-vitro diagnostic quantitative determination of free and protein bound salivary cortisol in human saliva as an aid in the assessment of Cushing Syndrome and Addison's Disease. Measurement s of cortisol in saliva are used in the diagnosis and treatment of disorders of the adrenal gland.	For the in-vitro diagnostic quantitative determination of free and protein bound salivary cortisol in human saliva as an aid in the assessment of Cushing Syndrome and Addison's Disease. Measurement s of cortisol in saliva are used in the diagnosis and treatment of disorders of the adrenal gland.
Analyte	Free and Protein-bound Cortisol	Free and Protein-bound Cortisol
Sample Type	Saliva	Saliva
Method	Enzyme immunoassay	Enzyme immunoassay
Detection Method	Colormetric microplate reader	Colormetric microplate reader
Test Principle	Cortisol in the sample competes with Cortisol-enzyme conjugate for binding sites to antibody bound to a microwell. Unbound components are washed away and enzyme is measured by a colored reaction with the TMB substrate.	Cortisol in the sample competes with cortisol-enzyme conjugate for binding sites to the antibody (rabbit anti cortisol) bound to a GARGG microplate. Unbound components are washed away and enzyme is measured by a colored reaction with the TMB substrate.
Calculations	Quantitative determination with standard curve	Quantitative determination with standard curve
Quality Control	Use of reference controls is recommended	Use of reference controls is recommended
Analytical Measuring Range (AMR)	0.12 ng/ml - 30.0 ng/ml	0.1 ng/ml – 30.0 ng/ml
Expected Values (Normal range)	N=192 Ages: 18-70 AM range: 0.8 – 15.5 ng/ml PM range: <0.12 – 3.6 ng/ml	N=152 Ages: 23 – 68 AM range: 2.58 – 12.69 ng/ml PM range: 0.25 – 2.96 ng/ml
Limits of Detection	Limit of Blank (LoB) not calculated	Limit of Blank (LoB) 0.0392 ng/ml

	Limit of Detection (LoD) not calculated Limit of Quantitation (LoQ) not calculated	Limit of Detection (LoD) 0.0519 ng/ml Limit of Quantitation (LoQ) 0.0519 ng/ml
Saliva Collection Device	Polypropylene vials and Salimetrics oral swab (SOS), Item # 5001.02	VWR Sample Mailing Tube Cat #16465-260
Interferences	Information not available in Salimetric's package insert	An in-vitro spiking study with high doses of caffeine, food, nicotine, alcohol and chewing gum did not reveal significant interference in the measurement of cortisol in saliva using the Pantex AM/PM Salivary Cortisol EIA Kit Cat #631.
Stability and Storage of Kit Reagents (open vial)	Stated as stable at 2°-8°C until the kit's expiration date	The stability of the opened kit reagents were determined to be 31 days when stored at 2°-8°C using Pantex AM/PM Salivary Cortisol EIA Kit Cat #631.

Test Summary:

Performance Characteristics-

The performance characteristics of Pantex AM/PM Salivary Cortisol Enzyme Immunoassay were based on evaluations by the following analytical performance tests.

I. Analytical Performance
  Precision/Repeatability
    Intra-assay
    Inter-assay
    Inter-lot variation
  Linearity
  Recovery
  Traceability, Reagent Stability, Sample Stability and Expected values
  Detection Limits
  Analytical Specificity/Cross Reactivity
II.Method Comparison

III. Interferences

I. Analytical Performance
a. Precision/Reproducibility

(i) The intra-assay precision was determined from 20 replicates of low, medium and high samples.

Sample	N	Mean (ng/mL)	Standard Deviation (ng/mL)	%CV
Low	20	0.627	0.034	5.4
Medium	20	3.995	0.266	6.7
High	20	25.232	1.579	6.3

(ii) The inter-assay precision was determined from the mean of average duplicates for twelve (12) separate assays.

Sample	N	Mean (ng/mL)	Standard Deviation (ng/mL)	%CV
Low	12	0.587	0.037	6.3
Medium	12	4.163	0.301	7.2
High	12	25.126	0.712	2.8

(iii) The inter-lot or between-lot variation was determined by duplicate measurements of five (5) pools of saliva samples and three (3) saliva controls using three (3) different lots. The results of intra-assay, inter-assay and inter-lot variation concluded a %CV of ≤10% for each sample tested.

Saliva samples	**Lot #012**	**Lot #013**	**Lot #014**	**Inter-lot**	**Inter-lot**	**Inter-lot**
ID	**Mean (ng/ml)**	**Mean (ng/ml)**	**Mean (ng/ml)**	**Mean (ng/ml)**	**Std.Dev. (ng/ml)**	**CV (%)**
20	4.65	4.45	4.79	4.64	0.164	3.5
21	0.67	0.61	0.71	0.67	0.049	7.4
22	2.02	1.95	2.09	2.02	0.069	3.4
23	4.75	4.69	4.76	4.73	0.041	0.9
24	2.01	1.99	2.04	2.01	0.026	1.3
25	3.64	3.67	3.71	3.68	0.036	1.0
LC	0.98	0.94	1.01	0.98	0.036	3.7
NC	5.21	5.31	5.49	5.34	0.140	2.6
HC	10.79	10.13	10.52	10.48	0.329	3.1

(iv) Repeatability

This study was conducted during 4 days of familiarization period and 20 days of testing. Two assays were performed daily with a minimum of 2 hours between assays. Three (3) different reagents lots and three (3) saliva pools were used for the study (Low, medium and high concentration). The pools were aliquoted and frozen until day of assay.

Repeatability Low Concentration	
Concentration (ng/ml)	0.600
Standard Deviation	0.0141
(I) (User Variance/Claim Variance) x R	62.695
(II) Critical Chi-square	65.171
Claim Rejected (I>II)	No
Claim Accepted (I<II)	Yes

Precision Low Concentration Pool		
	Standard Deviation, SD)	**(% Coefficient of Variation CV)**
Within Run	0.0224	3.79
Between Run	0.0462	7.80
Repeatability	0.0162	2.73
Total Device Precision	0.0538	9.09

Repeatability Medium Concentration	
Concentration (ng/ml)	4.0 ng/ml
Standard Deviation	0.0.894
(I) (User Variance/Claim Variance) x R	63.073
(II) Critical Chi-square	65.171
Claim Rejected (I>II)	No
Claim Accepted (I<II)	Yes

Precision Medium Concentration Pool		
	Standard Deviation, SD)	**(% Coefficient of Variation CV)**
Within Run	0.1475	3.60
Between Run	0.0514	1.26
Repeatability	0.1025	2.50
Total Device Precision	0.1869	4.56

Repeatability High Concentration	
Concentration (ng/ml)	25 ng/ml
Standard Deviation	0.5477
(I) (User Variance/Claim Variance) x R	62.035
(II) Critical Chi-square	65.171
Claim Rejected (I>II)	No
Claim Accepted (I<II)	Yes

Precision High Concentration Pool		
	Standard Deviation, SD)	**(% Coefficient of Variation CV)**
Within Run	0.4442	1.176
Between Run	0.2915	1.15
Repeatability	0.62276	2.46
Total Device Precision	0.8185	3.24

b. Linearity

Ten (10) sample concentrations that span the assay measuring range were performed Per EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures.

S=10 samples (dilutions)
Concentration = (C1*V1 + C10*V10)/(V1+V10)

	C1 ng/ml	V1 ng/ml	C10 ng/ml	V10 ng/ml	Calculated Concentration ng/ml	Obtained Concentration ng/ml	Recovery %
1	0.093			*	0.100	0.093	93.0
2	0.093	0.889	33.788	0.111	3.833	3.729	97.3
3	0.093	0.778	33.788	0.222	7.573	7.620	100.6
4	0.093	0.667	33.788	0.333	11.313	10.842	95.8
5	0.093	0.556	33.788	0.444	15.054	14.350	95.3
6	0.093	0.444	33.788	0.556	18.827	18.313	97.3
7	0.093	0.333	33.788	0.667	22.568	21.547	95.5
8	0.093	0.222	33.788	0.778	26.308	24.694	93.9
9	0.093	0.111	33.788	0.889	30.048	30.459	101.4
10				*	35.000	33.788	96.5

*Targets of low and high sample concentrations

c. Recovery:

Ten (10) saliva samples containing different levels of endogenous cortisol were spiked with known quantities of cortisol and assayed.

Sample	Endogenous (ng/ml	Added (ng/ml)	Expected (ng/ml)	Observed (ng/ml)	Recovery (%)
1	0.493	0.250	0.743	0.739	99.5
2	0.878	0.500	1.378	1.291	93.7
3	1.551	1.000	2.551	2.641	103.5
4	1.850	2.000	3.850	3.958	102.8
5	0.936	4.000	4.936	4.951	100.3
6	1.042	8.000	9.042	9.394	103.9
7	0.691	16.000	16.691	17.165	102.8
8	0.622	20.000	20.622	19.997	97.0
9	2.057	24.000	26.057	24.938	95.7
10	0.348	28.000	28.348	28.943	102.1

d. Traceability/Reagent Stability/Sample Stability/Expected Values
The calibrators and controls are prepared from stock cortisol (Steraloids) and are gravimetrically weighed and prepared. Concentration of stock cortisol (Steraloids) concentrations were confirmed by comparison to NIST cortisol ($y=1.029\ x-0.2195$. $R^2=0.9924$)

Summary of the stability results

Real time stability studies are conducted to determine the reagent and kit shelf life (expiration date). Expiration date of the Pantex AM/PM Salivary Cortisol EIA Kit, Cat 631, is determined by results of shelf life studies and is based on the reagent that has the shorter assigned expiration day.

1. The reagents stored at 2-8°C are stable for 9 months; therefore, the expiration date of the kit components is established at 9 months from the manufacturing date. We are basing the 9 month stability claim based on the results obtained with the real time stability study when stored at 2-8°C, supported by the reagents stored at room temperature (20 -28°C) and in reference to the stress chart that predicts reagents year stability at +5°C, by Kennon, L. "Use of models in determining chemical pharmaceutical stability".

Sample stability

Four (4) stress conditions on freshly collected saliva revealed the following:

Storage	Room Temperature 20 – 30 °C	37 °C	2 – 8 °C	≤ -15 °C (7 freeze / thaw cycles)	≤ - 15 ° C (Long term)
Stability	Up to 7 days	Up to 7 days	Up to 7 days	Up to 7 days	Up to 180 days

Open vial and working Cortisol-HRP Conjugate solution stability determination.

Condition	Stability	Storage Temperature
Reagents. Open vial stability	31 days	2-8 °C
Working Cortisol-HRP conjugate solution	31 days	2-8 °C

Expected Reference Values:

The reference range was re-established by testing 152 male saliva samples and 152 female samples to have an equal number of male and female samples. The reference range and median were recalculated using CLSI C28-A3 as a guide. The following tables indicate the summary of the results

AM Expected Values:

Subjects (Number)	Subjects (Gender)	Age (Years)	AM Median (ng/mL)	AM Range (ng/mL)
152	76 Males 76 Females	23-68	6.70	2.58 - 12.69

PM Expected Values:

Subjects (Number)	Subjects (Gender)	Age (Years)	PM Median (ng/mL)	PM Range (ng/mL)
152	76 Males 76 Females	23-68	0.58	0.25 - 2.96

e. Detection Limits

The LoB (limit of the blank), the LoD (limit of detection) and the LoQ (limit of quantitation) were determined by generating one hundred and twenty (120) measurements each of "cortisol free free salvia and low level (<0.1 ng/ml) cortisol samples (Reference, CLSI EP17-A, protocols for Determination of Limits of Detection and Limits of Quantitation).

Limits of Blank (LoB) ng/mL	Limits of Detection (LoD) ng/mL	Limits of Quantitation (LoQ) ng/mL
0.0392	0.0519	0.0519

f. Analytical Specificity/Cross Reactivity

Cross-reactivity was determined by testing those compounds most like to interfere with the Pantex AM/PM Salivary Cortisol EIA Kit. The specificity of the antiserum was evaluated by evaluating the cross-reactivity expressed as ratios of concentration of unlabeled cortisol over the compound that displaces 50% of cortisol-enzyme conjugate from the antiserum.

Compound	**Spiked Concentration**	**% Cross-reactivity**
C-21 Steroids		
Cortisol	10,000 ng/ml	100.0000
17-OH-Progesterone	10,000 ng/ml	0.0284
Pregnenolone	10,000 ng/ml	0.0038
17-OH-Pregnenolone	10,000 ng/ml	0.0066
Progesterone	10,000 ng/ml	0.0079
Desoxycorticosterone	10,000 ng/ml	0.0517
11-Desoxycortisol	10,000 ng/ml	1.8133
Dexamethasone	10,000 ng/ml	0.0164
Cortisone	10,000 ng/ml	0.7600
Corticosterone	10,000 ng/ml	1.0847
Aldosterone	10,000 ng/ml	0.0070
C-19 Steroids		
Androstenedione	10,000 ng/ml	0.0038
Testosterone	10,000 ng/ml	0.0042
5αDHT	10,000 ng/ml	0.0019
DHEA-SO4	10,000 ng/ml	0.0031
Androstanedione	10,000 ng/ml	0.0028
C-18 Steroids		
Estradiol 17β	10,000 ng/ml	0.0024
Estradiol 17α	10,000 ng/ml	0.0003
Estrone	10,000 ng/ml	0.0010
Estriol	10,000 ng/ml	0.0015
Other structurally related steroids		
Dehydroisoandrosterone	1000 ng/ml	0.0076
6αmethyl-17-Hydroxyprogesterone	1000 ng/ml	0.1427
6β Hydroxycortisol	1000 ng/ml	1.7177
Prednisone	1000 ng/ml	1.0874
Prednisolone	1000 ng/ml	25.9001

At >10% cross reaction prednisolone is a potential interfering substance.

II. Method Comparison Studies

Tests were conducted for comparison between the Pantex AM/PM Salivary Cortisol EIA Kit, Cat and the predicate assay , Salimetrics HS Salivary Cortisol EIA. The cortisol results of 160 samples were compared . Comparison of the Pantex AM/PM Salivary Cortisol EIA Kit (new device) and the Salimetrics HS Salivary Cortisol EIA (predicate) demonstrated acceptable regression and correlation statistics and appears to be substantially equivalent to the FDA cleared predicate device.

Pantex AM/PM Salivary Cortisol EIA versus Salimetrics HS Salivary Cortisol EIA	
Linear Regression equation	$Y = 1.0269x + 0.0994$
Correlation (r^2)	0.9797

III. Interferences Studies.

An in-vitro experiment was performed by spiking three (3) levels of Cortisol (low, medium and high) with high concentrations of five (5) potentially interfering substances: alcohol, coffee (as caffeine), cigarette (as nicotine) and food and gum extracts. The results obtained appear to demonstrate no significant interference of the substances tested in this study with the measurement of Cortisol in saliva using the Pantex AM/PM Salivary Cortisol EIA Kit, Cat #631.

In-vitro experiment results:

Pools	**Potential Interferent Caffeine Added (ug/mL)**	**Obtained Value (ng/mL)**	**Recovery from Control (%)**
Low Pool	0	1.420	100
	800	1.444	101.7
	400	1.438	101.3
	200	1.477	104.0
Middle Pool	0	4.932	100
	800	5.143	104.3
	400	5.063	102.7
	200	4.539	92.0
High Pool	0	28.302	100
	800	26.010	91.9
	400	26.811	94.7
	200	27.563	97.4

Pools	Potential Interferent Food Added (mg/mL)	Obtained Value (ng/mL)	Recovery from Control (%)
Low Pool	0.000	1.345	100
	426	1.340	99.6
	213	1.332	99.0
	106.5	1.291	96.0
Middle Pool	0.000	4.739	100
	426	4.730	99.8
	213	4.834	102.0
	106.5	4.835	102.0
High Pool	0.000	26.447	100
	426	27.495	104.0
	213	26.283	99.4
	106.5	28.055	106.1

Pools	Potential Interferent NicotineAdded (ug/mL)	Obtained Value (ng/mL)	Recovery from Control (%)
Low Pool	0	1.362	100
	800	1.436	101.7
	600	1.437	101.3
	400	1.4345	104.0
	200	1.317	96.7
Middle Pool	0	4.871	100
	800	5.243	107.6
	600	5.258	107.9
	400	5.087	104.4
	200	5.155	105.8
High Pool	0	25.503	100
	800	27.033	106.0
	600	26.397	103.5
	400	25.642	100.6
	200	24.928	97.8

Pools	Potential Interferent Gum Added (mg/mL)	Obtained Value (ng/mL)	Recovery from Control (%)
Low Pool	0	1.289	100
	270	1.346	104.4
	135	1.286	99.8
	67.5	1.248	96.8
	33.75	1.280	99.3
Middle Pool	0	4.843	100
	270	4.957	102.4
	135	4.845	100
	67.5	4.712	97.3
	33.75	4.764	98.4
High Pool	0	28.367	100
	270	29.419	103.7
	135	29.247	103.1
	67.5	27.870	98.3
	33.75	28.216	99.5

Pools	Potential Interferent Ethanol Added (%)	Obtained Value (ng/mL)	Recovery from Control (%)
Low Pool	0	1.268	100
	0.025	1.267	104.4
	0.050	1.230	99.8
	0.100	1.213	96.8
Middle Pool	0	4.539	100
	0.025	4.403	102.4
	0.050	4.320	100
	0.100	4.490	97.3
High Pool	0	26.272	100
	0.025	28.362	108.0
	0.050	28.744	109.4
	0.100	28.750	109.4

Concluding Statement:

Taken together, the performance characteristics, comparison studies with a predicate device and acceptable statistical performance studies in this 510(k) submission demonstrates that the Pantex AM/PM Salivary Cortisol EIA Kit, Cat #631, is safe and effective for its intended use and is substantially equivalent to the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Pantex, Division of Bio-Analysis, Inc
c/o Romulo Garza
1701 Berkeley Street
Santa Monica, CA 90404

MAY - 8 2012

Re: k102841
Trade Name: Pantex AM/PM Salivary Cortisol Enzyme Immunoassay
Regulation Number: 21 CFR §862.1205
Regulation Name: Cortisol (hydrocortisone and hydroxycorticosterone) test system
Regulatory Class: Class II
Product Codes: NHG
Dated: April 3, 2012
Received: May 2, 2012

Dear Dr. Garza:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (301) 796-5760. For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance...

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm

Sincerely yours,

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K102841

Device Name: Pantex AM/PM Salivary Cortisol Enzyme Immunoassay

Indications For Use:

For the in-vitro diagnostic quantitative determination of free and protein bound salivary cortisol in human saliva as an aid in the assessment of Cushing Syndrome and Addison's Disease. Measurements of cortisol in saliva are used in the diagnosis and treatment of disorders of the adrenal gland.

Prescription Use X (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) 102841